

Notice of Allowability

Application No.

10/063,592

Applicant(s)

GODDARD ET AL.

Examiner

Claire M. Kaufman

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to the telephone interview of 11/17/06 for the Ex's Amd't and responses of 7/31/06+9/11/06.
2. ☒ The allowed claim(s) is/are 1-5.
3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) ☐ All b) ☐ Some* c) ☐ None of the:
 1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

* Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
 - (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
 - 1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
 - (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☒ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3. ☒ Information Disclosure Statements (PTO-1449 or PTO/SB/08),
Paper No./Mail Date 7/31/06, 9/14/06
4. ☐ Examiner's Comment Regarding Requirement for Deposit
of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☐ Interview Summary (PTO-413),
Paper No./Mail Date _____.
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 7/31/06 has been entered.

EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it **MUST** be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Kerry Taylor for AnneMarie Kaiser on 11/17/06.

The application has been amended as follows:

In the specification, add after the first paragraph containing the continuing data on the first page:

On November 20, 2006, a CD submission of the Sequence Listing was filed in compliance with the requirements of 37 C.F.R. 1.821(c). The CD contains one file, with the filename: "Sequence Listing - P3230R1C1.txt", file size: 437 KB, date created: October 24, 2006. The information submitted in this CD is incorporated by reference in its entirety.

The **Title** has been replace with the following:

Antibody to PRO1557 polypeptide encoded by a nucleic acid highly expressed in esophageal and kidney tumors

Reasons for Allowance

The following is an examiner's statement of reasons for allowance: The claims of the instant invention are directed to an antibody that specifically binds the isolated polypeptide of SEQ ID NO:82. The specification provides several asserted utilities beginning at page 93, including that the PRO polypeptides of the present invention may be differentially expressed in a diseased tissue as compared to a normal tissue of the same tissue type (page 140 and 142).

Applicant states at, for example, page 2 of the response (9/11/06) that the gene expression data in the specification, Example 18 (p. 140), shows that the mRNA associated with the PRO1557 polypeptide was more highly expressed in esophageal and kidney tumor tissue compared to normal esophageal and kidney tissue. Gene expression was analyzed using standard quantitative PCR amplification reactions of cDNA libraries isolated from different human tumor and normal human tissue samples. Identification of the differential expression of the PRO1557 polypeptide-encoding mRNA in tumor tissue compared to the corresponding normal tissue renders the molecule useful and enabled as a diagnostic tool for the determination of the presence or absence of tumor.

Example 18 at pages 140 and 142 of the instant specification demonstrates differential expression of PRO1557 cDNA using quantitative PCR amplification reactions. DNA64902-1667 was shown to be more highly expressed in esophageal and kidney tumor tissue compared to normal esophageal and kidney tissue in this Example. Applicant states at page 2 of the response that Example 18 utilizes an accurate and reliable method of assessing changes in mRNA levels, namely reverse transcriptase PCR (RT-PCR) analysis. Applicant relies on more than 40 references (see IDS filed 07/31/06 and 9/14/06), where expression levels of mRNA measured by RT-PCR were found to have a good correlation to the expressed protein levels.

It had been previously argued in the Examiner's Answer mailed 5/30/06 that mRNA levels were not predictive of protein levels, citing references by Haynes et al., Gygi et al., and Fessler et al. However, these references were measuring and analyzing mRNA levels using microarrays, not using quantitative PCR analysis; and, the art recognizes that the results obtained by microarray are less likely to have the same accuracy as those obtained using quantitative PCR (for example, see Oda et al., *Virchows Arch.* 430:99-105, 1997, *e.g.*, page 104,

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column 1, paragraph 2 (IDS filed 9/14/06); and Papotti et al., *Virchows Arch.* 440(5):461-75, 2002, e.g., p. 472, col.1, beginning of last paragraph (submitted in full herewith)). While the USPTO found references in which the protein expression levels did not correlate with mRNA levels measured by quantitative PCR (e.g., Toler et al., *Am. J. Obstet. Gynecol.* 194: e27-e31, 2006, and Berner et al., *Histopathol.* 42:546-554, 2003, cited in the IDS filed 9/14/06), the majority of the references which were found, including those cited by Applicant, demonstrated a correlation between mRNA levels measured by RT-PCR and protein expression levels.

Applicant asserts that the expression levels of protein correlate to mRNA (cDNA) levels when measured by quantitative PCR (*i.e.*, RT-PCR). Applicant has provided more than 40 references in support of this position. The prior art of record (Haynes et al., Gygi et al., Fessler et al.), argued by the Examiner, is not specifically directed to message levels measured by RT-PCR. Based on the totality of evidence of record, one of skill in the art would find it more likely than not that an increase in message as measured by RT-PCR would be predictive of an increase in protein expression levels, absent evidence to the contrary. Therefore, the data presented in Example 18, which demonstrates differential expression of nucleic acids encoding PRO1557, also supports a conclusion of differential expression of the PRO1557 polypeptide. Therefore, one of ordinary skill in the art would be able to use diagnostically for distinguishing esophageal and kidney tumors from normal esophagus and kidney tissue the PRO1557 polypeptide and antibody which specifically binds it, as asserted by Applicant.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Claire M. Kaufman, whose telephone number is (571) 272-0873. Dr. Kaufman can generally be reached Monday, Tuesday, Thursday and Friday from 9:30AM to 2:30PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, can be reached at (571) 272-0835.

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Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Official papers filed by fax should be directed to (571) 273-8300. NOTE: If applicant *does* submit a paper by fax, the original signed copy should be retained by the applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Claire M. Kaufman, Ph.D.



Patent Examiner, Art Unit 1646

November 21, 2006



LORRAINE SPECTOR
PRIMARY EXAMINER